BIOTECHNOLOGY REFRIGERATOR

The Biotechnology Refrigerator (BTR) is a thermoelectric, temperature controlled unit. It provides approximately 0.57 cubic feet (0.016 cubic meters) of refrigerated storage for temperature-sensitive cell science supplies and samples being used in or transported to space.

GAS SUPPLY MODULE

The Gas Supply Module (GSM) provides a blend of oxygen, nitrogen, and carbon dioxide to experiments at a delivery pressure of 40 psig. The premixed gas is provided through external hoses which connect the front panel of the GSM to a bioreactor or an incubator.

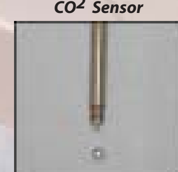
HYDRODYNAMIC FOCUSING BIOREACTOR

On-orbit, the formation of air bubbles in cell culture fluid, and attempts to remove them from the Space Bioreactor, disrupt the low shear culture environment and degrade three-dimensional tissue assemblies. The new **Hydrodynamic Focusing Bioreactor (HFB)** is designed to overcome these problems\characteristics. The HFB produces a low shear environment for culture of cell suspensions and tissue aggregates. A variable hydrodynamic force allows removal of air bubbles from the bioreactor vessel with little or no disruption in the environment.

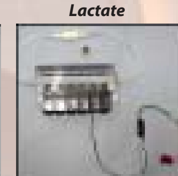
SENSORS

The next generation of bioreactors will include a battery of sensors that will further advance the ability of the bioreactor tissue culture systems to be used for tissue engineering on Earth and in space.

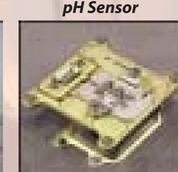
CO^{2} Sensor



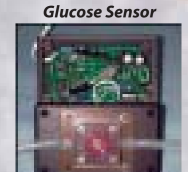
Lactate



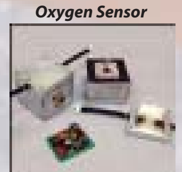
pH Sensor



Glucose Sensor



Oxygen Sensor



Investigators in medical, university, and industrial laboratories throughout the United States are using NASA-designed bioreactors on Earth and in space to grow cells into three-dimensional tissue-like structures. New insights gained from this technology are enhancing the fields of:

Medical Oncology - improved three-dimensional cancer models allow scientists to investigate the dynamics of cancer formation, progression and treatment.

Tissue Engineering - new processes to culture tissues potentially suitable for transplantation such as cartilage and cardiac tissues are being developed.

Pharmacology - the use of cellular aggregates makes possible novel processes to develop and test drug interactions.

Bacteriology and Virology - growing infectious agents such as viruses and parasites in human cells and tissues will aid in the elucidation of microbial pathogenesis and thereby facilitate the development of vaccines and antibiotics.

While the rotating bioreactor is providing researchers with new avenues of investigation in cell biology, it is also expected to contribute to our effort to extend human exploration of our solar system and beyond. Research conducted with the NASA bioreactors could lead to the production of biosensors that could be sent into space as exploratory probes. The response of these probes to microgravity could assist scientists in identifying medical risks that are unique to microgravity and in designing safe and effective countermeasures.

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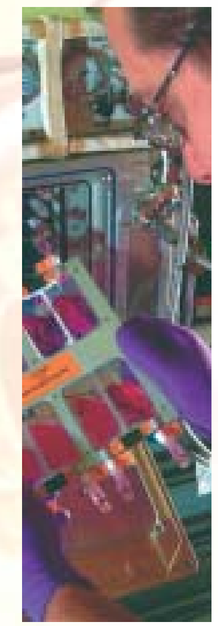
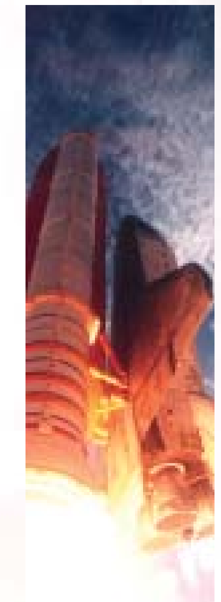




Cellular Biotechnology Program

NASA's microgravity-based, low shear bioreactor systems are enabling new approaches to and opportunities in biotechnology. The use of these technologies on Earth and in space are opening new vistas in the fields of tissue engineering, disease treatment, tissue modeling and drug development.

The Research

TISSUE MODELS

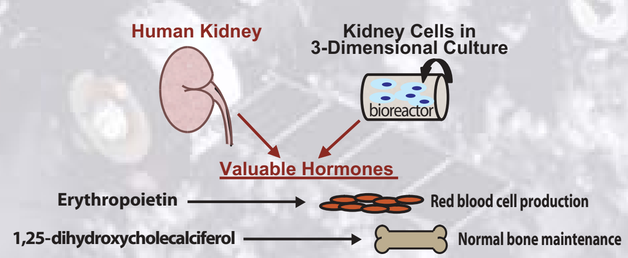
The unique low shear culture environment provided by NASA bioreactor technology enables the formation and maintenance of tissue homologs that demonstrate the following characteristics: assembly into cell aggregates, three-dimensional replication and growth, cellular differentiation and synthesis of extracellular matrix. Many important tissues have been produced using bioreactor technology such as pancreatic, liver, cartilage, cardiac and kidney tissues.

Tissue homologs have a high structural and functional fidelity to *in vivo* tissue and are used by many scientists throughout the U.S. for basic and biomedical research. In addition, three-dimensional carcinoma tissue models are under development for scientists to use for understanding carcinogenesis and metastasis. These models may also be utilized in investigations that will lead to improved chemotherapeutic and immunotherapeutic treatments.

BIOPHARMACEUTICALS

NASA bioreactor technology and microgravity-based cell culture is an emerging platform for production of biologically significant molecules. Bioreactor technology provides a unique culture environment in which cellular functions involved in the growth of cells and tissues and the expression of cellular products and receptors can be studied and controlled. Scientists are beginning to use this low shear force technology to enhance our understanding and control of cells and tissues for the production of valuable bio-products.

The kidneys provide, among their many functions, several important hormones that are required to maintain normal physiological function. Patients with dialysis-dependent end-stage renal disease often require replacement of the kidney hormones erythropoietin (EPO) and 1-25 dihydroxycholecalciferol (1-25diOH-D3), which are some of the most expensive pharmaceuticals in the world. **Dr. Timothy Hammond** of Tulane University has used NASA bioreactor technology in space (STS-86, STS-90, STS-105, ISS 7A.1, ISS UF-1) to develop a three-dimensional renal tissue model that produces these hormones. This model offers great promise as an experimental model and as a source of renal hormones for potential clinical pharmacological therapy.

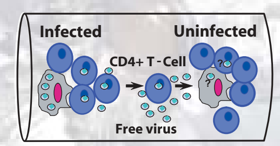


HIV SCHEMATIC

Dr. Joshua Zimmerberg of the NASA/National Institutes of Health (NIH) Center for Three-Dimensional Tissue Culture produced an exciting model which permits the study of HIV pathogenesis using two components of the lymphoid system: the lymphoid tissue itself and the circulating lymphocytes. The progression of HIV pathogenesis is a complex interaction of specific tissues, cells and the virus. The NASA/NIH group successfully used a NASA-designed bioreactor system to maintain blocks of human lymphoid tissues that were infected with laboratory strains of HIV-1 for up to three weeks. With this system, investigators have learned that Langerhans cells ferry HIV to lymphoid tissue, where the virus can infect CD4 cells (AIDS. 2000;14:647-651).

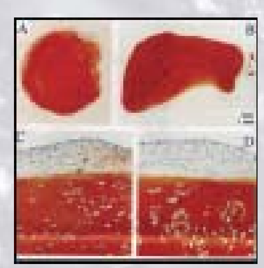
THREE-DIMENSIONAL LYMPHOID MODEL

Lymphoid tissue (gray), lymphoid T-cells (blue), and HIV virus (purple), represent the major components of a lymphoid tissue model developed at the NASA/NIH Center using NASA bioreactor technology. NIH scientists are using this model to investigate the mechanism by which the virus is transmitted from one tissue site to another within a human host. The ability to simultaneously sustain both the large three-dimensional lymphoid tissue and the circulating lymphoid cellular components may enable scientists to identify and understand the key cell interactions that enable viral transmission.

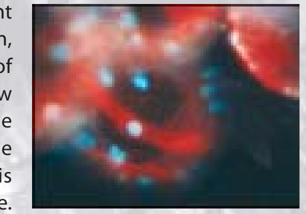


TISSUE ENGINEERING

Millions of Americans suffer tissue or organ loss from disease or accident. Presently, the only treatments for these losses include maintenance strategies and transplantation. These approaches are severely limited by high cost and donor shortages. A substantial need exists for the development of alternative strategies. NASA bioreactors can be used to cultivate engineered tissues from isolated cells and three-dimensional polymer scaffolds. On Earth, by adjusting the vessel rotation speed, tissue constructs can be maintained in a state of continual free-fall. The relatively well-defined fluid dynamic conditions stimulate cells within constructs to mature and form structural and functional associations characteristic of tissue.



Dr. Lisa Freed of the Massachusetts Institute of Technology tested the hypothesis that microgravity affords specific advantages in the formation of cartilage from cultured cells. Cells seeded onto synthetic scaffolds were propagated continuously in the NASA bioreactor on Mir for more than 130 days. Cartilage formed in both space and ground-based bioreactors. The cartilage formed in space was spherical, less dense, and substantially more compressible than that grown on the ground. The tissue grown on Earth adapted the disc-like morphology of the



Dr. Robert Akins of the A.E. duPont Hospital for Children in Wilmington, Delaware is investigating the use of the NASA bioreactor systems to grow functional heart tissue from single cells. Three-dimensional cardiac tissue formed in the bioreactor is architecturally similar to native tissue. The new cardiac tissue structures contracted spontaneously, and were responsive to treatments with cardio-active drugs.

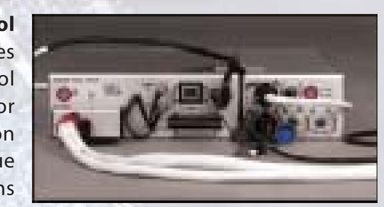
The Hardware

ROTATING WALL PERFUSED SYSTEM

The Rotating Perfused System (RWPS) is a bioreactor system used to grow three-dimensional tissue cultures in space.

EXPERIMENT CONTROL COMPUTER

The Experiment Control Computer (ECC) provides the computer control resources required for automated, long-duration cell culture and tissue engineering investigations on-orbit.



BIOTECHNOLOGY SPECIMEN TEMPERATURE CONTROLLER

The Biotechnology Specimen Temperature Controller (BSTC) is a static bulk incubator bioreactor designed to maintain a homeostatic environment for cell growth. The BSTC supports multiple cell culture experiments simultaneously. Multiple cell lines are grown within individual Teflon bags called Tissue Culture Modules (TCM). Compared to the rotating vessel bioreactors, the BSTC typically grows cultures for a limited time (~14 days).